roles, however, should not preclude the recognition of a role for methyl groups in the dynamics of biomolecules.

3710-Pos Board B571
Modeling Polymer Interactions with Nanopores for DNA Sequencing and Proteomics Applications
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Protein beta-barrel nanopores have been used to characterize a wide variety of molecules including polyethylene glycol (PEG), deoxyribonucleic acid (DNA) and polypeptides - a potentially significant step in realizing low cost sequencing of DNA, as well as in proteomics. Simulations can improve our understanding of the conformation and dynamics of polymers inside a nanopore, which we believe are significant to properly interpret experimental data. However, in an effort to overcome the limitations of time scales associated with all-atom molecular dynamics simulations we introduce two simplified models for PEG in α-hemolysin. Both represent the nanopore by a grid potential calculated from the Poisson-Boltzmann equation, and contain explicit ions and flexible PEG. One model includes water implicitly with a short-range water mediated potential of mean force to correctly account for ion-ion interactions; the other contains explicit TIP3 water. We also present a third, even simpler model with rigid PEG in the pore, where the ionic current blockade differs from experiment significantly highlighting the importance of the dynamics of PEG inside the pore. We then compare results from the first two simulation models with those from an all-atom simulation. Finally, we compare the depth of the ionic current blockade associated with PEG binding from each model with experimental results.

3711-Pos Board B572
Simulations of DNA Bending using Adaptive Umbrella Sampling on Roll Angles
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Many proteins bend DNA significantly upon binding. To simulate this bending within the time scales accessible to molecular dynamics, we used adaptive umbrella sampling on the roll angles. We studied the inherent flexibility of bare DNA by simulating dodecamers with varying sequences and made comparisons to the worm-like chain model. Simulations of bare DNA were also performed to assess the co-operativity of the bending of adjacent roll angles. A study of DNA bending by the archaeal DNA packaging protein Sac7d will be presented as well.

3712-Pos Board B573
Computational Modeling of Telomerase in Action
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Telomerase is a special reverse transcriptase that adds repetitive DNA sequences, GGGTTG for *Tetrahymena thermophila*, at the 3' end of DNA strand in the telomere region to ensure DNA replication completion. This enzyme is a ribonucleoprotein complex with RNA subunit as a template for synthesis of the repetitive telomeres. Telomerase is a key element to understand cellular aging and tumorigenesis due to its direct impact on chromosome length maintenance. The mechanism with which telomerase adds the six nucleotide repeat is not well-understood with current experimental biochemical and biophysical methods. The lack of three-dimensional structure of telomerase further hinders the current effort to fully understand its crucial biological function. Here, we attempt to propose a 3D structural model of the six catalytic steps using computational modeling with experimental constraints. We perform discrete molecular dynamics simulations with experimental constraints derived from SHAPE chemistry, FRET and crystal structure homology modeling. Our preliminary results reveal interesting structural features and dynamic properties of telomerase in action. Further simulations and detailed computational analysis will allow us to generate experimentally testable hypothesis. The synergetic approaches of computational modeling and experimental validation will help us understand the molecular mechanism of telomerase.

3713-Pos Board B574
Deriving Transferable Parameters for the Coarse-Grained Martini Model: Application to Amyloid-Like and Elastin-Like Peptides
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Coarse-grained (CG) models provide a computationally efficient means for investigating complex biological processes over relatively long periods of time and length scales at a reduced level of detail. We present recent advances on our extension of the CG MARTINI model to more accurately describe backbone flexibility of proteins by introducing in the energy function a term that accounts for the dihedral potentials on the peptide backbone. The modified model is applied to amyloid-like and elastin-like peptides, and its performance is assessed from its ability to reproduce structural properties calculated from atomistic trajectories of peptides in water. The transferability of dihedral potentials is addressed in terms of peptide length since it is significantly more challenging to obtain complete conformational sampling for longer peptides compared to shorter peptides. We test the transferability of dihedral parameters by employing parameters derived from the atomistic trajectories of shorter fragments in simulations of longer peptides. Our results show that transferable parameters can be derived to model long peptides with the modified CG MARTINI model.

3714-Pos Board B575
Effect of Mutations on Aβ Monomer Flexibility: Implications for Peptide Association
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Aggregates of the amyloid beta peptide (Aβ) are thought to trigger brain cell death in Alzheimer's disease patients. The current hypothesis is that Aβ aggregation occurs after the peptide is released from the cell membrane to the aqueous environment. Two different types of Aβ aggregates have been identified: soluble and insoluble. Soluble aggregates are formed in early stages of peptide association, whereas insoluble aggregates are the final state of aggregation. Interestingly, it is the soluble aggregates, not the insoluble ones, which correlate with disease progression. Despite the relevance of soluble aggregates as a target for Alzheimer's disease, their mechanism of formation is unknown. The formation of soluble aggregates in solution is strongly affected by mutations in the Aβ sequence. The role of local flexibility in protein function has recently received attention: in this study we ask whether local flexibility plays a similar role in soluble aggregate formation. To answer this question, we perform all-atom molecular dynamics simulations of the wild-type Aβ(1-40) monomer in water, and two mutated forms (Q15L & D23Y) that vary in their ability to form soluble aggregates. Our results show that the flexibility of the monomer is linked to the quantity of soluble aggregates formed: the more flexible peptide, D23Y, displays fewer soluble aggregates. Its enhanced flexibility could allow the peptide to more easily access the conformations most favorable to association and nucleation. Since Aβ aggregation and toxicity increase with peptide length, we compare monomer flexibility for the Aβ(1-40) peptides with their respective Aβ(1-42) analogues. The dynamic patterns are not conserved between the Aβ(1-40) and Aβ(1-42) versions; this suggests that mutations may affect Aβ monomer flexibility differently depending on its length.

3715-Pos Board B576
Adsorption of the Full Length Amyloid Beta Peptide on the Carbon Nanotube Surface and the Thermodynamic Implications for Fibrillogenesis
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Nanomaterials such as carbon nanotubes have gained recent attention, in part due to their potential applicability in biology and medicine. However, there are relatively few studies at the single-molecule level that explore the interactions of nanomaterials with biological building blocks such as peptides and proteins. Using fully atomistic molecular dynamics (MD) simulations at physiological temperatures, we have investigated the mechanism of adsorption of the full length, 42-residue, monomeric Amyloid beta peptide on the surface of a single walled carbon nanotube (SWCNT) of small diameter. Starting with different relative orientations of the peptide and the SWCNT that delineate the interactions arising from different important segments of the peptide, we find rapid convergence in the peptide's adsorption behavior within tens of nanoseconds, manifested in the arrested movement of the peptide in the nanotube's vicinity, in the convergence between the peptide-nanotube contact areas and approach distances, and in the observed increase of peptide curvature around the nanotube. Probing the interactions of different residue segments with the SWCNT, we find that the peptide's adsorption is initiated by interactions